Overweight and obesity: a concise review for clinicians

Excesso de peso e obesidade: uma revisao concisa para clínicos

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Abstract

Overweight and obesity continue to rise being highly prevalent throughout the world, and are related to an unbalance between energy intake and output. Genetic, endocrine, neuroendocrine, behavioral and environmental factors play an important role in their etiopathogenesis. The diagnosis is made based on the body mass index and waist circumference. The prevention and treatment are necessary, since an excessive morbidity and mortality can be linked to obesity and its associated disorders mainly cardiovascular and metabolic. Proper nutrition and increased physical activity are the main focus of these measures. Adjuvant pharmacological intervention (orlistat) is recommended for patients with concomitant overweight- or obesity-related diseases and for whom diet and physical activity have not been successful. Bariatric surgery is reserved for patients with severe obesity or those with moderate obesity associated with a serious medical condition, after at least one year of an inefficient conservative treatment. The purpose of this review is to assess all these aspects.

Key words: overweight and obesity, body mass index, waist circumference, diet and exercise, orlistat, bariatric surgery.

Resumo

O excesso de peso e a obesidade têm vindo a aumentar contìnuamente, são extremamente frequentes em todo o mundo, e resultam do desequilíbrio entre o consumo e a utilizaçao de energia. Factores genéticos, endócrinos, neuroendócrinos e ambientais têm um papel importante na sua etiopatogenia. O diagnóstico é feito, avaliando o índice de massa corporal e medindo o perímetro da cintura. Deve-se efectuar a prevenção e o tratamento sempre que o excesso de morbilidade e mortalidade seja atribuído à obesidade e às suas consequências, sobretudo cardiovasculares e metabólicas . A alimentação adequada e o aumento do exercício físico são as principais medidas. A farmacoterapia (orlistat) é indicada para os doentes com complicações orgânicas devido ao excesso de peso ou à obesidade, e também para quem a dieta e o exercício físico não foram eficazes. Apenas nos casos de obesidade mórbida ou moderada com comorbilidades graves, depois de pelo menos um ano de tratamento conservador sem resultados, se deve recorrer à cirurgia bariátrica. O presente trabalho de revisão tem o objectivo de examinar todos estes aspectos.

Palavras chave: excesso de peso e obesidade, índice de massa corporal, perímetro da cintura, dieta e exercício físico, orlistat, cirurgia bariátrica.

INTRODUCTION

Overweight and obesity are most commonly found all over the world. Their many medical consequences are responsible for an excessive morbidity and mortality. Therefore, the prevention and treatment of overweight and obesity are necessary. This review will inform about prevalence, diagnosis, etiopathogenesis, consequences, prevention, and treatment of overweight and obesity.

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PREVALENCE

In the last thirty years, the prevalence of overweight among children, adolescents and adults has increased continuously all over the world. Approximately 1.7 billion people worldwide are overweight and at least 300 million of them are obese. These data have been announced by the International Obesity Task Force (IOTF), a collaborative program of the International Association for the Study of Obesity (IASO) and the World Health Organization (WHO), recently.[1,2]

In the U.S., more than 60 million adults, or 1 in every 3, are obese.[3,4] According to data published by the IOTF in 2007,[5,6] the highest estimates of obesity prevalence in adults was found in Nauru (80 % in men and 78 % in women), followed by Lebanon (36 % in men and 38 % in women), the United States (31 % in men and 33 % in women), Croacia (31 % in men and 15 % in women), and Panama (28 % in men and

36 % in women); the lowest prevalence rates were seen in Africa, where the highest rates were found in South Africa (10 %) and Seychelles (9 %); however, even countries such as Ghana show a prevalence of 20% among women.

An adult populational survey in Portugal from 2003 to 2005 showed for overweight a prevalence of 39.4 % and for obesity 14.3 %.[7]

The recently published "Nationale Verzehrsstudie II" (NVS) found in adult German population an obesity prevalence of 20.5 % in men and 21.2 % in women for the year 2006.[8]

A relative obesity prevalence increase of 39 % in men and 44 % in women in the last 20 years was found in Germany.[8] Such increases have been seen worldwide. In the USA, however, for men only, whereas there were no significant increases among women.[4]

Also, many countries all over the world, developed and developing alike, have observed an increase in the prevalence of overweight and obesity among children and adolescents; 34 countries were studied; at least 10 % of youth were overweight, and in 20 % of the countries at least 3 % were obese; the prevalence of overweight and obese youth is particularly high in North America, Great Britain and southwestern European countries; the highest rate was found in Malta and the lowest one in Lithuania.[9]

An Indian population study found the prevalence of obesity as well as overweight higher in boys as compared to girls (12.4 % *vs* 9.9 %, 15.7 % *vs* 12.9 %).[10]

A survey showed a prevalence of 13.1 % for overweight and of 4.9 % for obesity in German children.[11]

DEFINITION AND DIAGNOSIS

Overweight and obesity refer to the condition in which excess fat has accumulated in the body.

The most common method of determining weight status is the body mass index (BMI). This measure relates an individual's weight to his or her height. BMI is the weight in kilograms divided by the square of the height in meters. According to the WHO classification,[12,13] subjects with a BMI between 25 and 29.9 kg/m^2 are defined as overweight and those with a BMI equal to or over 30 kg/m^2 as obese *(Table I)*.

Abdominal skinfold measures, waist-to-hip ratio (WHR) and waist circumference are considered to be markers of central obesity or intra-abdominal fat.[12,13]

Waist circumference in combination with BMI has shown to be the best descriptor of obesity and predictor of risks for cardiovascular and metabolic, and other disorders; a waist size greater than 102 cm for men and 88 cm for women increases the risk for most weight-related diseases.[12,13] In persons with BMI equal to or over 25 kg/m^2 , the waist size should be always measured.[12]

TABLE I

Classification of overweight and obesity by BMI (WHO, 2000)

	Obesity class	BMI (kg/m^2)
Underweight		Lower than 18.5
Normal		18.5 – 24.9
Overweight		25.0 – 29.9
Obesity	I	30.0 – 34.9
	II	35.0 – 39.9
Extreme obesity	III	Equal to or over 40.0

With respect to the clinical management of children and adolescent obesity, an accurate measurement of BMI and waist circumference should be compared with the age and gender appropriate BMI and waist circumference percentiles curves. The Centers for Disease Control and Prevention (CDC) and IOTF in the United States, and many countries have developed such charts.[9]

Furthermore, we have to consider that Asians are particularly vulnerable to obesity-related diseases, with rising rates of comorbidities from BMI 23 kg/m^2; therefore, the WHO has recommended that the optimal BMI for Asian population shall be narrowed to 18.5-23 kg/m^2.[2]

The measure of waist-to-hip-ratio (WHR) is also used. Values greater than 0.9 for men and greater than 0.85 for women may be predictor of pathologic consequences of obesity.[12,13]

Other methods for measuring body fat include using electronic impulses, water tank submersion, scanning techniques such as computed tomography (CT) or magnetic resonance imaging (MRI) or dual-energy x-ray absorptiometry (DEXA) and special scales; thus, abdominovisceral-to-subcutaneous ratio (vis/sc ratio) can be determined; a vis/sc ratio > 0.4 is associated with significantly higher risk for metabolic disorders than a vis/sc ratio < 0.4 (subcutaneous

TABLE II

Factors implicated in the etiopathogenesis of overweight and obesity

Genetic factors
Environmental and behavioral factors
Imbalance between energy intake and energy expenditure
Various hormones, peptides, and biological factors

accentuation of body fat).[14] These new techniques, although providing more precise measure of body fat, are costly and therefore reserved for investigation work and impractical for clinical use.[13,14]

ETIOPATHOGENESIS

The following factors are involved in the etiopathogenesis of overweight and obesity *(Table II):*

Genetic factors

Overweight and obesity are commonly found in families. Identical twins have very similar BMIs, and their BMIs are much more strongly correlated than those of dizygotic twins. Inheritance is usually not Mendelian. Monogenetic causes of obesity are very rare, and these were found mainly in children. Melanocortin-receptor-4-(MC4R-)gene mutations have a prevalence of up to 5 % in children obesity. Recently, a variant of FTO-gene has been identified which is associated with an elevated BMI in children and adults. We hope that new studies on single nucleotid polymorphisms (SNP) would be useful to explain properly the genetic etiology of obesity.[1, 14-18]

Environmental and behavioral factors

The recent increase in the prevalence of obesity, worldwide, is far too rapid to be due to genetic etiology. Availability and composition of nutrition and changes in the level of physical activity are very important. Obesity is related to behaviors that lead to increased food intake or decreased energy expenditure. High fat-diets may promote obesity, especially in combination with diets rich in simple carbohydrate. It is well known that famine prevents obesity. Obesity is more often found among poor women in developed countries; on the other hand, it is more common among wealthier women in underdeveloped countries. Children obesity correlates to some extent with time spent watching television. Some studies suggest that sleep deprivation leads to increased obesity. Human obesity seems to be less a metabolic than a neuro--behavioral disease.[1,17,18]

Energy intake and energy expenditure

Overweight and obesity are related to an imbalance between energy intake and expenditure.

After a long term positive energy imbalance, obesity develops, especially in subjects with a genetic predisposition.

A correct measurement of energy intake is nearly impossible in free-living individuals; obese, in particular, often underreport intake of energy. Energy expenditure can be determined using doubly labeled water or metabolic chamber/rooms.

There is a physiologic mechanism centered around a sensing system in adipose tissue that reflects fat stores and a receptor, or "adipostat", that is in the hypothalamic centers. When fat stores are abundant, the signal is increased, and the hypothalamus responds by decreasing hunger and increasing energy expenditure. On the other hand, when fat stores are depleted, the adipostat signal is low, and the hypothalamus leads to stimulate hunger and decrease expenditure of energy to conserve energy. The *ob* gene, and its product leptin, and the *db* gene, and its product leptin receptor, provide important elements of a molecular basis for this physiologic concept.

These compensatory mechanisms frequently fails in obese; therefore, hyper-caloric nutrition and low physical activity develop obesity; a 0.3 % positive energy imbalance over 30 years would result in a 9 kg weight gain; in subjects at stable weight, intake of energy equals energy expenditure.[1,12,14,17]

Leptin

Leptin is a cytokine-like polypeptide produced by the adipocyte that controls food intake through activation of hypothalamic receptors; it increases energy expenditure via sympathetic activation in thermogenic and nonthermogenic tissues. Obese individuals have a leptin resistance, leptin levels are increased, there is no mutations of either leptin or its receptor; some authors suggest that these subjects produce less leptin per unit fat mass than others or have a form of relative leptin deficiency; the mechanism for leptin resistance, and whether it can be overcome by raising leptin levels, is not yet established; according to some data, it may be that leptin does not cross the blood-brain barrier as

levels rise; animal studies suggest that leptin signaling inhibitors, such as suppressor of cytokine signaling 3 (SOCS3) and proteine tyrosine phosphatase (PTP1b), are involved in the leptin-resistant state.[1,17,19]

Neuropeptide Y

Neuropeptide Y (NPY), as well as Agouti-related peptide (AgRP), alpha-melanocyte-stimulating hormone (alpha-MSH), and melanin-concentrating hormone (MCH) are hypothalamic peptides. They are integrated with catecholaminergic, endocannabinoid, opioid, and serotoninergic signaling pathways. In addition, NPY is one of the most potent stimulators of food intake, together with other peptides like MCH, and growth hormone releasing hormone (GHRH). It is likely that leptin modulates the expression of NPY that helps to control the drive to consume excess food. The highest plasma NPY levels are observed in obese hypertensive and diabetic subjects.[1,17]

Ghrelin and other gut peptides

Ghrelin is a gut peptide, highly concentrated in the stomach; it increases appetite and stimulates feeding; ghrelin secretion increases with fasting and decreases in the postprandial phase. Surprisingly, plasma ghrelin levels are reduced in obese humans. The effect of ghrelin on weight is probably mediated through central antagonism of leptin and other anorectic cytokines. Ghrelin is also a growth hormone secretagoge.[1,17,20]

Other gut peptides, such as cholecystokinin (CCK), enterostatin, intestinal hormones peptide YY, pancreatic polipeptide, glucagon-like peptide-1 (GLP-1), and oxyntomodulin regulate energy homeostasis, suppressing food intake, and subsequently decreasing energy intake.[1,17,20,21]

Insulin

Insulin is secreted by the beta cells of the pancreas; it is an anabolic hormone, directing the storage and utilization of energy in the adipocytes. Obesity is related to hyperinsulinemia and insulin resistance. The molecular link between obesity and insulin resistance in tissues, such as fat, muscle, and liver has been sought for many years. Increased body weight reduces moderately hepatic and periphereal liver sensitivity. Insulin resistance is more strongly linked to intraabdominal fat than to fat in other depots. Resistin, a fat cell peptide, selectively expressed in white adipose tissue, encodes a protein that is increased by diet-induced or genetic forms of obesity, and is decreased with weight loss or treatment with thiazolidinediones. Leptin, adiponectin (one of the adipocytokines expressed in fat tissue) and immunoneutralization of resistin improve insulin sensitivity. Tumor necrosis factor-alpha (TNF-alpha) and resistin may facilitate insulin resistance.[1,14,17,22,23]

Cortisol

Cortisol is a glucocorticoid hormone, produced by suprarenal gland. During stress situations, subjects have high cortisol levels and eat larger quantities of food and significantly more sweet foods. Cushing syndrome is associated with elevated visceral or abdominal fat. It seems that the hypothalamic-pituitary-adrenal (HPA) axis works in concert with acute increases in insulin after feeding, and leads to elevated visceral adipose tissue storage.[1,17]

Other hormones and biological factors are implicated in obesity, at present without clinical significance, further research should clarify their role. The brain endocannabinoid system seems to control food intake via mediators of appetite, and through reinforcing motivation to find and consume foods with high incentive value.[1,17]

PATHOLOGIC CONSEQUENCES

Overweight and obesity are associated with an excess in mortality, with a 50-100 % increased risk of death from all causes compared to normalweight individuals. Obesity and overweight together are the second leading cause of preventable death in the USA, accounting for 300,000 deaths per year. Mortality rates rise as obesity increases, particularly in abdominal obesity. Life expectance of a moderately obese individual could be shortened by 2-5 years, and a 20- to 30- year-old man with a BMI over 45 may lose 13 years of life.[1,9,17,24] Medical consequences of obesity are listed in *Table III*.

Metabolic syndrome

It has a prevalence of 23.8 % (21.0 % for women and 26.6 for men) in Germany. Although the metabolic sydrome is known for many years, an international approved definition exists, since 1998. In the meantime, there are 5 definitions, worldwide. Considering these data, metabolic syndrome should include following metabolic factors: abdominal obesity, insulin resistance (hyperinsulinemia and glucose

TABLE III

Pathologic consequences of overweight and obesity

Metabolic syndrome
Type 2 diabetes
Nonalcoholic fatty liver disease
Cardiovascular disease
Pulmonary disease
Gallstones
Osteoarthritis and skin disorders
Malignancies
Reproductive disorders

intolerance or elevated blood glucose), dyslipidemia (low HDL cholesterol and high triglycerides), raised blood pressure; furthermore, high fibrinogen and elevated C-reactive protein (CRP) suggest an inflammatory state.[1,9,14,17,24]

Type 2 diabetes

About 70 % of subjects with type 2 diabetes have a BMI of 30 kg/m^2 or greater. The prevalence of type 2 diabetes is nearly 5 times higher for men and 8.3 times higher for women in obese population compared to normal weight persons. A gain in weight of 7.0-10.9 kg in adolescents and adults leads to a twice the risk of developing type 2 diabetes. However, approximately 70 % of obese individuals do not develop type 2 diabetes, despite nearly universal insulin resistance. This finding suggests that the diabetes manifestation requires an interaction between obesity-induced insulin resistance and other factors that predispose to diabetes, such as impaired insulin secretion.[1,9,14,17,24]

Nonalcoholic fatty liver disease

The prevalence of nonalcoholic fatty liver disease (NAFLD) is estimated to range between 10 % and 24 % in the general population; it ranges between 70 % and 90 % in type 2 diabetes subjects. Insulin resistance facilitates the occurrence of NAFLD, as well as of obesity, type 2 diabetes and dyslipidemia. Recently, NAFLD has been included among components of the metabolic syndrome, increasing the risk of cardiovascular disease. According to the American Association for the Study of Liver Diseases, it is necessary for the diagnosis that the alcohol consumption is not more than 20 g/d; furthermore, it must be found by liver biopsy more than 5 % hepatic steatosis; other relative sensitive diagnostic methods may include the computer tomography (CT) , magnet resonance imaging (MRI) or ultrasonography. Elevated values for plasma concentrations of high-sensitivity C--reactive protein (hs-CRP), fibrinogen, plasminogen activator inhibitor-1 (PAI-1) activity, and adiponectin are found in NAFLD patients compared to nonobese healthy subjects.[25,26]

Cardiovascular disease

The effects of obesity and overweight affect cardiovascular disease (CVD), and include atherosklerosis, arterial hypertension, coronary heart disease (CHD), congestive heart failure (CHF), arrhythmias, stroke, sudden death, and peripheral vascular disease (PVD). According to the results of Framingham Study, obesity is an independent risk factor for the 26-year incidence of CVD. Obesity, especially abdominal obesity, is associated with an atherogenic lipid profil, decreased levels of the vascular protective adipocytokine adiponectin, and obesity-induced hypertension. Arterial hypertension leads to increased peripheral resistance and cardiac output, increased sympathetic nervous system tone, elevated salt sensitivity, and insulin-mediated salt retention. Leptin may mediate through sympathetic activation the obesity-induced hypertension.[1,9,14,17,19,24]

Pulmonary disease

Many pulmonary abnormalities may be found associated to obesity, such as reduced chest wall compliance, elevated work of breathing, increased minute ventilation, and decreased functional residual capacity and expiratory reserve volume. About 10-15 % of morbidly obese patients may develop the obesity-hypoventilation syndrome (OHS) with attenuated hypoxic and hypercapnic ventilatory responses. Severe obesity may be associated with obstructive sleep apnea (OSA), and these patients suffer commonly from hypertension. A weight gain of as little as 10 % has predicted a six-fold increase in the odds of developing sleep-disordered breathing; a loss of 10 % body weight predicted a 26 % decrease in the apnea-hypopnea index; a weight loss of 10-20 kg can improve substantially these pulmonary and sleep disorders in obese population.[1,17]

Gallstones

It is found an increased risk of gallstones in persons

with increasing BMI. A person 50 % above ideal body weight has approximately a six-fold increased incidence of symptomatic gallstones. Obese undergoing bariatric surgery has as high as a 43 % incidence of gallbladder disease, defined as prior cholecytectomie or gallstones. The gallstone formation requires secretion of supersaturated bile composition and gallbladder stasis. Obesity is associated with these both conditions. More saturated bile due to cholesterol hypersecretion leads to the impairment of gallbladder motility. Recent studies suggest that leptin may mediate the association between obesity and gallstones.[1,17]

Osteoarthritis and skin disorders

The gout prevalence is increased in obesity. The increased joint load and indirect metabolic alterations (high plasma values for cholesterol, glucose and uric acid) lead to osteoarthritis. The adjusted risk of knee osteoarthritis is increased fourfold in men with a current BMI between 23 kg/m^2 to < 25 kg/m^2 as compared to men with BMI < 23 kg/m^2. The most common skin alterations related to obesity is acanthosis nigricans. The skin folds are getting dark and thick on the neck, elbows, and dorsal interphalangeal spaces. Friability of skin is increased in these regions, enhancing the risk of fungal and yeast infections. Acanthosis nigricans reflects the severity of underlying insulin resistance and diminishes with weight loss. The increased venous stasis in the obese leads to peripheral varicosis and its complications, such as thrombophlebitis and varicose ulcer.[1,17]

Malignancies

Cancer of the esophagus, colon, rectum, pancreas, liver, and prostata are the cause of higher mortality in obese males. Obesity in females is associated with higher mortality from cancer of the gallbladder, bile ducts, breasts, endometrium, cervix and ovaries. Some of the genital cancers in females may be due to increased rates of conversion of androstenedione to estrone in adipose tissue. Recent data in the USA estimate that obesity accounts for 14 % of cancer deaths in men and 20 % in women.[12,17]

Reproductive disorders

Increased levels of gonadotropins and biologically active free androgens may cause anovulation in females. Obesity is associated with menstrual disorders. Common findings in women are elevated androgen production, reduced sex hormone-binding globulin (SHBG), and increased peripheral conversion of androgen to estrogen. The polycystic ovarian syndrome (PCOS), associated with anovulation and ovarian hyperandrogenism, is found frequently. PCOS patients are insulin-resistant, and have hyperinsulinemia, suggesting that both these factors are responsible for the etiopathogenesis of PCOS. Weight loss and insulin-sensitizing drugs often restore normal menstruation. Obesity after pregnancy results in pronounced and sustained weight gain due to exogeneous factors, like hyper-caloric nutrition, lower physical activities, and drug abuse. Infertile, obese women with abnormal follicle-stimulating hormone (FSH) levels have significantly lower chances of pregnancy.[1,17]

In obese men testosterone and SHBG are decreased, and due to conversion of adrenal androgens in adipose tissue, estrogen levels are increased. Gynecomastia may be found. However, mostly, no alteration occurs in masculinization, libido, potency, and spermatogenesis. Free testosterone may be reduced in extreme obese men.[1,17]

PREVENTION AND TREATMENT

These measures are necessary to improve overweight- and obesity-related diseases, reduce the risk of developing further comorbidities, and recover the decreased quality of life.[12,14,27]

A literature search identified 64 preventions programs seeking to produce weight gain prevention effects in children and adolescents, of which only 21 % were effective.[28] Only a few healthy-weight and overweight adults receive these primary prevention.[29]

Future trials may show better results, since new community strategies have been recommended in the USA and Europe.

The U.S. 24 strategies are divided into six categories: 1) strategies to promote the availability of affordable food and beverages, 2) strategies to support healthy food and beverage choices, 3) a strategy to encourage breastfeeding, 4) strategies to encourage physical activity or limit sedentary activity among children and youth, 5) strategies to create safe communities that support physical activity, and 6) strategies to encourage communities to organize for change.[30]

According to the recent guidelines of the German Diabetes Association (DDG), the prevention should be aimed at a stabilization of body weight, possibly at

TABLE IV

Treatment of overweight and obesity

	BMI kg/m²				
Treatment	**25-26.9**	**27-29.9**	**30-35**	**35-39.9**	**Equal to or over 40**
Diet, exercise, behavioral modification	With co-morbidities	With co-morbidities	+	+	+
Adjuvant medication	–	With co-morbidities	+	+	+
Bariatric surgery	–	–	–	With co-morbidities	+

the normal weight level, while the mean body weight of adults increases continuously until 65 years age; a moderate decrease of body weight is indicated in subjects with BMI between 25 and 29.9 kg/m^2; regular exercise, preferably moderate stamina physical activity, everyday, is recommended, as well as a balanced nutrition with moderate fat, more starch, dietary fiber, and low-energy dense foods.[12,14,27]

Therapy should begin with a proper diet, physical activity and behavioral management, and may include pharmacological intervention or surgery. Setting an initial weight-loss goal of 5-10 % over 6 months is a realistic target.[12,27] Indications and different treatments are outlined in *Table IV.*

Diet

A calorie deficit of 500-800 kcal/d compared to the individual's habitual nutrition is recommended. This deficit should be achieved by reduction of fat; the daily fat intake should be kept between 20 and 35 % of daily calories, and there is no need of decreasing carbohydrate intake. Thus, it can be achieved a weight decrease of 1-2 lb per week, 5-10 % after 6 months and a long-term weight stabilization.[12,14,27]

For a longer period, a balanced diet of 1200-2000 kcal/d, depending on weight, exercise, gender and age is recommended. This diet should contain moderate fat, more starch, and more dietary fiber. It is suggested a daily fiber intake of 38 g (men) and 25 g (women) for persons over 50 years of age and 30 g (men) and 21 g (women) for those under 50.[12,27]

Diets of 800-1200 kcal/d reduce stronger the body weight. In this case, subjects have to drink water, at least 2.5 l/d. Low-calorie diets should be carried out under medical care, and not longer than 12 weeks. This method is indicated for cases in which a rapid weight reduction is necessary because of medical reasons.[12]

The calorie deficit can be achieved by choosing smaller portion sizes, eating more vegetables and fruits, consuming more whole-grain cereals, selecting leaner cuts of meat and skimmed dairy products, reducing fried foods and other added fats and oils, and drinking water instead of caloric beverages.[27]

Low-carbohydrate diets (e.g., South Beach, Zone, and Sugar Busters!) are based on the concept that carbohydrates are the primary cause of obesity and lead to insulin resistance. The recommended carbohydrate level corresponds to 40-46 % of energy. After these diets, there is a rapid and good decrease of body weight. Long-term results are lacking.[12,27]

The Atkins diet contains 5-15 % carbohydrate, depending on the phase of the diet. This diet does not limit the intake of fat and animal protein. Many randomized, controlled trials demonstrated greater weight loss at 6 months. Weight loss between groups did not remain statistically significant at 1 year. However, low-carbohydrate diets seem to be at least as effective as low-fat diets in inducing weight loss for up to 1 year.[1,27]

The concept of energy density should be considered. The energy density refers to the number of calories a food contains per unit of weight. People tend to ingest a constant volume of food, regardless of caloric or macronutrient content. Adding water or fiber to food decreases its energy density by increasing weight without affecting caloric content. Foods with low-energy density include soups, fruits, vegetables, oatmeal, and lean meats. Dry foods and high-fat foods like pretzels, cheese, egg yolks, potato chips, and red meat have a high-energy density. Diets containing low-energy dense foods control hunger, decrease caloric intake, and induce weight loss.[27]

All these diets have shown an improvement in coronary heart disease risk factors, including an increase in HDL cholesterol and a decrease in triglyceride

levels. Also a decrease of systolic and diastolic blood pressure has been found.[1,9,12,14,27]

Very-low-calorie diets of less than 800 kcal/d, and total fasting promote a rapid and significant short--term weight loss. These measures have been now abandoned because of higher medical risks.[12,27]

Paradoxically, fasting and very-low-caloric diets may induce cholecystitis and cholecystolithiasis.[1,17] The risk for gallstone formation increases considerably at rates of weight loss >1.5 kg/week. This risk can be reduced by administrating ursodeoxycholic acid, 600 mg/d.[1,27]

Exercise

Measures to increase exercise include reinforcement of physical activity and limitation of sedentary time. At least 30 min/d of moderate-intensity exercise should be recommended, initially. Increased physical activity can be achieved by slight modifications of the normal daily routine. Examples include walking, using the stairs, doing home and yard work, and engaging in sport activities. A useful strategy is that the subject wears a pedometer to monitor total accumulation of steps as part of the activities of daily living. There is a high correlation between step counts and activity level. The main role of exercise seems to be in the maintenance of weight loss achieved by low-calorie diet. Exercise alone is only moderately effective for weight loss.[1,9,12,14,27]

The Dietary Guidelines for Americans 2005 suggests at least 60-90 min/d moderate-intensity physical activity for sustaining weight loss. Intensity of exercise should be increased gradually from a low level to higher level, considering the poor cardiorespiratory fitness of these individuals. According to the American College of Sports Medicine, overweight and obese persons should increase progressively to a minimum of 150 min/week of moderate-intensity exercise as a first goal; for long-term weight loss, 200-300 min/week is needed. Consultation with an exercise physiologist or personal trainer may be helpful.[1,9,12,27]

Behavioral therapy

The theory of planned behavior is very useful for the treatment of overweight and obesity. Following independent constructs determine behavioral intentions: perceived behavioral control, subjective norm (perceived social pressure to perform the behavior), and attitude (positive-negative evaluations of behavior). Thus, people are more likely to reinforce new dietary and exercise behaviors if they have a positive attitude towards these both therapy measures, if they perceive social pressure, and they believe they will be successful. Strategies include self-monitoring techniques (e.g., weighing, measuring food and activity, and journaling); stress management; stimulus control (e.g., using smaller plates, not eating in front of the television or in the car); social support; problem solving; and cognitive restructuring to help patients develop more positive and realistic thoughts about themselves. When recommending any behavioral lifestyle change, have the patient identify what, when, where, and how the behavioral change will be performed. The patient should keep a record of the anticipated behavioral change so that the progress can be reviewed at the next office visit. These techniques are often provided by ancillary office staff such as a nurse clinician or registered dietitian because these methods are time-consuming.[1,12,14,27]

Adjuvant pharmacotherapy

This therapy can be indicated for some overweight and obese subjects *(Table IV)*. Currently, there is only one strategy for this adjuvant pharmacotherapy: reduction of the absorption of selective macronutrients from the gastrointestinal (GI) tract, such as fat. This can be achieved by using orlistat (Xenical®). This substance is a synthetic hydrogenated derivative of a naturally occurring lipase inhibitor, lipostatin, produced by the mold *Streptomyces toxytricini*. Orlistat is a potent, slowly reversible inhibitor of pancreatic, gastric, and carboxylester lipases and phospholipase A2, which are required for the hydrolysis of dietary fat into fatty acids and monoacylglycerols. This substance binds convalently with the active site of these lipases in the lumen of the stomach and small intestine. Orlistat, taken at a dose of 120 mg 3 times a day, blocks the digestion and absorption of circa 30 % of dietary fat.[1,12,27]

Several randomized, 1-2 year double-blind, placebo-controlled studies demonstrated that after one year, orlistat produces a main weight loss of 2-4 kg, i.e., about 9-10 %, compared with a 4-6 % weight loss on placebo.[27]

Orlistat is < 1 % absorbed; therefore, it has no systemic side effects. Its tolerability is related to the malabsorption of dietary fat and subsequent passage of fat in the feces. At least 10 % of orlistat-treated in-

dividuals have GI tract adverse effects. These include flatus with discharge, fecal urgency, fatty/oily stool, and increased defecation. These troubles are generally observed early, and diminish as subjects control their dietary fat intake, or take psyllium mucilloid concomitantly with orlistat. Serum concentrations of the fat-soluble vitamins D und E and beta-carotene may be reduced in 5-15 % of cases, such cases need vitamin supplements.[1,12,27]

The use of orlistat should be continued, only in case of a weight loss of at least 2 kg within first 4 weeks of treatment. The therapeutic efficacy and safety of this drug has been demonstrated for 2-4 years. Therefore, the administration beyond this time period is not recommended.[12]

Finally, we have to mention the substance P (SP), a peptide belonging to the tachykinin family of peptides. It is expressed in the central nervous system and in peripheral tissues, including the GI and respiratory tracts, the urinary and immune systems, blood wessels, adipose tissue and skin. SP exerts its various effects via its high affinity neurokinin-1 receptor (NK-IR). Injection of SP into normal mice showed a mild, dose-dependent increase in food intake together with an increase in the expression of neuropeptide Y and a decrease in the expression of the anorexigenic peptide, pro-opiomelanocortin. Mice treated with NK-IR antagonists reduced their food intake and lost weight. These findings indicate that SP is orexigenic in mice and that NK-IR antagonists may represent a potential target against obesity.[31]

Surgery

Bariatric surgery can be an option for some individuals *(Table IV)*, after at least one year of an inefficient conservative therapy. Surgical weight loss occurs by reducing caloric intake and, depending on the procedure, macronutrient absorption. There are two categories of weight-loss surgeries: restrictive and restrictive-malabsorptive. The restrictive procedures like vertical banded gastroplasty (VBG) and laparoscopic adjustable silicone gastric banding (LASGB) limit the amount of food the stomach can hold and slow the rate of gastric emptying. The restrictive--malabsorptive interventions, e.g. Roux-en-y gastric bypass (RYGB), biliopancreatic diversion (BPD), and biliopancreatic diversion with duodenal switch (BPDDS) combine the elements of gastric restriction and selective malabsorption. All these interventions can be performed laparoscopically or operative, depending on the surgeon's experience and health condition of the patient.[1,12,14,27]

VBG, in which a small pouch with a restricted outlet is constructed along the lesser curvature of the stomach, is currently performed on a very limited basis because of lack of effectiveness in long-term trials.

LASGB has replaced the VBG. An inflatable band is placed around the upper stomach to create a small pouch and narrow passage into the remainder of the stomach. The diameter of this band is adjustable by way of its connection to a reservoir that is implanted under the skin. Increasing or decreasing the amount of salt solution in the reservoir tightens or loosens the internal diameter of the band, and the size of the gastric passage.

RYGB, the most commonly performed and accepted bypass intervention, in which a proximal gastric pouch is constructed whose outlet is a Y-shaped limb of the small intestine.

BPD, a procedure less frequently used, in which a large part of the stomach is removed, the small pouch that remains is connected directly to the final segment of the small intestine, completely bypassing other parts of the small intestine; bile and pancreatic digestive juices mix in a remainig common chanel prior to entering into the colon; weight loss occurs since most of the nutrients are routed into the colon where they are not absorbed.

BPDDS, a variation of BPD, not commonly used, includes a "duodenal switch", which leaves a larger portion of the stomach intact, including the pyloric valve that regulates the release of gastric contents into the small intestine; also a small part of duodenum remains.

Restrictive-malabsorptive procedures generally produce a 30-35 % average body weight loss that is maintained in nearly 60 % of patients at 5 years. Restrictive interventions lead to lower weight loss, circa 20-30 kg at 24 months. In addition, many studies support the benefits of bariatric surgery for obesity-related comorbidities, such as type 2 diabetes, hypertension, obstructive sleep apnea, dyslipidemia, and nonalcoholic fatty liver disease.

Surgical mortality from bariatric surgery varies with the procedure, patient's age and comorbidities, and is generally < 1 %. The most common surgical complications, occurring in 5-30 % of patients, include GI leaks from the breakdown of the staple or suture

line, stomal obstruction or stenosis or marginal ulcers, bleeding, infection, gallstones, pulmonary embolism, respiratoy failure. Also a "dumping syndrome" (not after BPDDS) may be observed; this happens when the stomach contents move too rapidly through the small intestine. For subjects who undergo VBG or LASGB, there are no intestinal absorptive abnormalities other than mechanical reduction of gastric size and outflow. In contrast, RYGB, BPD, and BPDDS may lead to deficiencies of vitamin B_{12}, iron, folate, calcium, and vitamin D. In such cases, lifelong supplementation with these micronutrients is necessary.[1,12,27]

LONG-TERM LIFESTYLE INTERVENTIONS

Long-term lifestyle modifications (diet, physical activity, behavior therapy) are necessary for permanent results of weight management (weight loss and prevention of weight gain). These interventions produce weight improvement, the prevention or amelioration of arterial hypertension and other cardiovascular risk factors, and reduction of risk for type 2 diabetes and the metabolic syndrome.[32]

Furthermore, according to the recent guidelines of the German Diabetes Association (DDG)[12] the following factors must be considered:

- The energy balance must continually be kept under control. A return to the previous lifestyle leads to weight gain;
- A low-fat diet appears to be proper for the prevention of weight gain;
- Physical activity increases energy consumption, and maintains the muscle mass;
- Regular contact between patient and therapist is necessary for continual motivation;
- Integration into a self-help group and the support of family or other close persons prevent weight gain.
- Regular weight monitoring (once a week) and self--management have positive effects.

CONCLUSION

Overweight and obesity are the ever rising epidemics worldwide, and are strongly associated with major adverse consequences for human health and quality of life. The simple method of determining weight status is the measurement of body mass index along with size of waist circumference and waist-to-hip ratio. Changes in behavioral factors, decreased physical activity, and over-consumption of high-fat and energy--dense foods are the important etiological causes. Furthermore, it must be considered that persons, having some genetic and biological predisposition, exposed to an unfavorable environment, may gain weight. Clinicians should screen all patients for overweight and obesity and offer them intensive counseling about the basic treatment with proper diet, exercise, and behavioral modifications to promote sustained weight loss. Adjuvant medications or bariatric surgery are further options for non-responders to basic program. The principal goal of treatment is to improve comorbidities and lifestyle. Research advances raise hopes for more effective primary prevention. ■

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References

1. Wilborn C, Beckham J, Campbell B et al. Obesity: Prevalence, Theories, Medical Consequences, Management, and Research Directions. J Int Soc Sports Nutr 2005; 2: 4-31.

2. Deitel M. Overweight and Obesity Worldwide now Estimated to Involve 1.7 Billion People. Obesity Surgery 2003; 13: 329-330.

3. Ma J, Xiao L, Stafford RS. Adult Obesity and Office-based Quality of Care in the U.S. Obesity 2009; 17: 1077-1085.

4. Ogden CL, Carrol MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. JAMA 2006; 295: 1549-1555.

5. Aranceta J, Moreno B, Moya M, Anadón A. Prevention of overweight and obesity from a public health perspective. Nutr Rev 2009; 67: S83-S88.

6. International Obesity Task Force. The Global Challenge of Obesity and the International Obesity Task Force. Available at: http://www.iuns.org/features/obesity/tabfig.htm. Accessed 10 September 2007.

7. do Carmo I, dos Santos O, Camolas J et al. Overweight and obesity in Portugal: national prevalence in 2003-2006. Obes Rev 2008; 9: 11-19.

8. Hauner H, Bramlage P, Lösch C et al. Übergewicht, Adipositas und erhöhter Taillenumfang. Dtsch Ärztebl 2008; 105: 827-833.

9. Jolliffe CJ, Janssen I. Vascular risks and management of obesity in children and adolescents. Vasc Health Risk Manag 2006; 2: 171-187.

10. Chhatwal J, Verma M, Riar SK. Obesity among pre-adolescent and adolescents of a developing country (India). Asia Pac J Clin Nutr 2004; 13: 231-235.

11. Weber E, Hiebl A, Storr U. Prävalenz und Einflussfaktoren von Übergewicht und Adipositas bei Einschulungskindern. Dtsch Ärztebl 2008; 105: 883-889.

12. Hauner H, Buchholz G, Hamann A et al. Adipositas und Diabetes mellitus. Praxis-Leitlinien der Deutschen Diabetes-Gesellschaft. Diabetologie 2009; 4: S144-S149.

13. Wilk EA. Overweight. Definition and scope. Available at: http://www.euphix.org/object_document/o4619n27195.html. Accessed 7 September 2009.

14. Blüher M, Hamann A. Adipositas und metabolisches Syndrom. Diabetologie 2008; 3: R1-R18.

15. Hebebrand J, Friedel S, Schäuble N et al. Perspectives: molecular genetic research in human obesity. Obes Rev 2003; 4: 139-146.

16. Frayling TM, Timpson NJ, Weedon MN et al. A common variant in the FTO gene is associated with body mass index und predisposes to childhood and adult obesity. Science 2007; 316: 889-894.

17. Flier JS, Maratos-Flier E. Biology of Obesity. In Fauci AS, Braunwald E, Kasper DL, et al. eds. Harrison's Online. Featuring the complete contents of Harrison's Principles of Internal Medicine, 17e.

18. O'Rahilly S, Farooqi IS. Genetic of obesity. Philos Trans R Soc Lond B Biol Sci 2006; 361: 1095-1105.

19. Bravo PE, Morse S, Borne DM, Aguilar EA, Reisin E. Leptin and Hypertension in Obesity. Vasc Health Risk Manag 2006; 2: 163-169.

20. Murphy KG, Dhillo WS, Bloom SR. Gut peptides in the regulation of food intake and energy homeostasis. Endocr Rev 2006; 27: 719-727.

21. Gallwitz B. Betazellen, Inseln und Inkretine. Diabetologie 2007; 2: R11-R24.

22. Steppan CM, Bailey ST, Bhat S et al. The hormone resistin links obesity to diabetes. Nature 2001; 409: 307-312.

23. Fasshauer M, Klein J, Blüher M, Paschke R. Adipokine: Mögliches Bindeglied zwischen Insulinresitenz und Adipositas. Dtsch Ärztebl 2004; 101: 2792-2795.

24. Cameron AJ, Dunstan DW, Owen N et al. Health and mortality consequences of abdominal obesity: evidence from the AusDiab study. MJA 2009; 191: 202-208.

25. Stefan N, Kantartzis K, Häring H.-U. Die frühe Fettleber und ihre Folgen. Diabetologie 2008; 3: 105-111.

26. Lizardi-Cervera J, Aguilar-Zapata D. Nonalcoholic fatty liver disease and its association with cardiovascular disease. Ann Hepatol 2009; 8: S40-S43.

27. Kushner RF. Evaluation and Management of Obesity. In Fauci AS, Braunwald E, Kasper DL et al. eds. Harrison's Online. Featuring the complete contents of Harrison's Principals of Internal Medicine, 17e.

28. Stice E, Shaw H, Marti CN. A Meta-Analytic Review of Obesity Prevention Programs for Children and Adolescents: The Skinny on Interventions that Work. Psychol Bull 2006; 132: 667-691.

29. Lutfiyya MN, Nika B, Ng L, Tragos C, Won R, Lipsky MS. Primary Prevention of Overweight and Obesity: An Analysis of National Survey Data. J Gen Intern Med 2008; 23: 821-823.

30. Khan LK, Sobush K, Keener D et al. Recommended community strategies and measurements to prevent obesity in the United States. MMWR Recomm Rep 2009; 58: 1-28.

31. Karagiannides I, Torres D, Tseng Y-H et al. Substance P as a novel anti--obesity target. Gastroenterology 2008; 134: 747-755.

32. Brown T, Avenell A, Edmunds LD et al. Systematic review of long-term lifestyle interventions to prevent weight gain and morbidity in adults. Obes Rev 2009; 10: 627-638.